

Substitute for Form 1449 A &amp; B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 1 of 4

**Complete if Known**

Application Number	10/066,657
Confirmation Number	5724
Filing Date	February 06, 2002
First Named Inventor	Daniel JAVITT
Art Unit	1617
Examiner Name	Theodore J. Criares
Attorney Docket Number	A8311

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		Number	Kind Code <sup>2</sup> (if known)		
K		US 4,904,681		2/1990	Cordi et al.
K		US 5,260,324		11/1993	Cordi et al.
K		US 5,187,171		2/1993	Cordi et al.
K		US 5,068,412		11/1991	Ohfuno et al.
K		US 5,086,072		2/1992	Trullas et al.
K		US 5,179,085		1/1883	Bigge et al.
K		US 5,428,069		6/1995	Skolnick et al.
		US			
		US			

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Translation <sup>6</sup>
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>2</sup> (if known)			

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city, and/or country where published.	Translation <sup>6</sup>
K		Bergeron R, Meyer T M, Coyle J T, Greene R W. Modulation of N-methyl-D-aspartate receptor function by glycine transport. Proc Natl Acad Sci USA. 1998;95:15730-4.	
K		Danysz W, Parsons C G. Glycine and N-methyl-D-aspartate receptors: Physiological significance and possible therapeutic applications. Pharmacol. Rev. 1998;50:597-664.	
K		Debler E A, Lajtha A (1987): High-affinity transport of gamma-aminobutyric acid, glycine, taurine, L-aspartic acid, and L-glutamic acid in synaptosomal (P2) tissue: a kinetic and substrate specificity analysis. J Neurochem 48:1851-6.	
K		D'Souza D C, Charney D, Krystal J (1995): Glycine site agonists of the NMDA receptor: a review. CNS Drug Revs 1:227-260.	
K		Hashimoto A, Oka T, Nishikawa T (1995): Extracellular concentration of endogenous free D-serine in the rat brain as revealed by in vivo microdialysis. Neuroscience 66:635-643.	
K		Hashimoto A, Oka T (1997): Free D-aspartate and D-serine in the mammalian brain and periphery. Prog. Neurobiol 52:325-353.	

Examiner Signature	<i>g/h/h '16</i>	Date Considered	<i>06/29/05</i>
--------------------	------------------	-----------------	-----------------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov), MPEP 901.04 or in the comment box of this document. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to indicate here if English language Translation is attached.

Substitute for Form 1449 A &amp; B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 2 of 4

**Complete if Known**

Application Number	10/066,657
Confirmation Number	5724
Filing Date	February 06, 2002
First Named Inventor	Daniel JAVITT
Art Unit	1617
Examiner Name	Theodore J. Criares
Attorney Docket Number	A8311

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		Number	Kind Code <sup>2</sup> (if known)		
		US			
		US			

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Translation <sup>6</sup>
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city, and/or country where published.	Translation <sup>6</sup>
K		Heresco-Levy U, Javitt D C, Irmilov M, Mordel C, Horowitz A, Kelly D (1996): Double-blind, placebo-controlled, crossover trial of glycine adjuvant therapy for treatment-resistant schizophrenia. Br J Psychiatry 169:610-617.	
K		Javitt D C, Sershen H, Hashim A, Lajtha A (1997): Reversal of phencyclidine-induced hyperactivity by glycine and the glycine uptake antagonist glycyldodecylamide. Neuropsychopharmacol 17:202-204.	
K		Javitt D C, Frusciant M J. (1997): Glycyldodecylamide, a phencyclidine behavioral antagonist, blocks cortical glycine uptake: Implications for schizophrenia and substance abuse. Psychopharmacol. 129: 96-98.	
K		Javitt D C, Zylberman I, Zukin S R, Heresco-Levy U, Lindenmayer J P (1994): Amelioration of negative symptoms in schizophrenia by glycine. Am J Psychiatry 151:1234-1236.	
K		Javitt D C, Zukin S R (1991): Recent advances in the phencyclidine model of schizophrenia. Am J Psychiatry 148:1301-8.	
K		Javitt D C, Zukin S R (1989): Interaction of [sup.3H]MK-801 with multiple states of the N-methyl-D-aspartate receptor complex of rat brain. Proc. Nat. Acad. Sci. USA. 86:740-744.	
K		Javitt D C (1987): Negative schizophrenic symptomatology and the phencyclidine (PCP) model of schizophrenia. Hill J Psychiat 9:12-35.	
K		Kleckner N W, Dingledine R (1988): Requirement for glycine in the activation of NMDA-receptors expressed in Xenopus oocytes. Science 241:835-837.	
K		Leiderman E, Zylberman I, Javitt D C, Zukin S R, Cooper T B. Effect of high-dose oral glycine on serum levels and negative symptoms in schizophrenia. Biol. Psychiatry, in press.	
K		Liu Q R, Lopez-Corcuera B, Mandiyan S, Nelson H, Nelson N (1993): Cloning and expression of spinal cord- and brain-specific glycine transporter with novel structural features. J Biol Chem 268:22802-8.	

Examiner Signature	<i>Shelton</i>	Date Considered	06/29/05
--------------------	----------------	-----------------	----------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kind Codes of USPTO Patent Documents at www.uspto.gov, MPEP 901.04 or in the comment box of this document. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to indicate here if English language Translation is attached.

Substitute for Form 1449 A &amp; B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 3 of 4**Complete if Known**

Application Number	10/066,657
Confirmation Number	5724
Filing Date	February 06, 2002
First Named Inventor	Daniel JAVITT
Art Unit	1617
Examiner Name	Theodore J. Criares
Attorney Docket Number	A8311

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		Number	Kind Code <sup>2</sup> (if known)		
		US			
		US			

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Translation <sup>6</sup>
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			

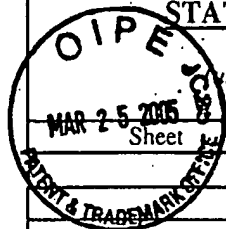
**NON PATENT LITERATURE DOCUMENTS**

Ks		Matsui T, Sekiguchi M, Hashimoto A, Tomita V, Nishikawa T, Wada K (1995) Functional comparison of D-serine and glycine in rodents: the effect on cloned NMDA receptors and the extracellular concentration. J Neurochem. 65:454-458.	
Ks		McBain C J, Kleckner N W, Wyrick S, Dingledine R (1989): Structural requirements for the glycine coagonist site of N-methyl-D-aspartate receptors expressed in Xenopus oocytes. Mol Pharmacol 36:556-565.	
		Murray F, Kennedy J, Hutson P H, et al (2000): Modulation of [3H]MK-801 binding to NMDA receptors in vivo and in vitro. Eur J Pharmacol 397:263-70.	
Ks		Reynold I J, Murphy S N, Miller R J (1987): 3H-labeled MK-801 binding to the excitatory amino acid receptor complex from rat brain is enhanced by glycine. Proc. Natl. Acad. Sci. USA 84:7744-7748.	
Ks		Schell M J, Molliver M E, Snyder S H (1995). D-serine, an endogenous synaptic modulator: localization to astrocytes and glutamate-stimulated release. Proc. Natl. Acad. Sci. USA 92:3948-3952.	
Ks		Sershen H, Latha A (1995): Inhibition pattern by analogs indicates the presence of ten or more transport systems for amino acids in brain cells. J Neurochem 32:719-726.	
Ks		Smith K E, Borden L A, Hartig P R, Branchek T, Weinshank R L (1992): Cloning and expression of a glycine transporter reveal colocalization with NMDA receptors. Neuron 8:927-35.	
		Supplisson S, Bergman C (1997): Control of NMDA receptor activation by a glycine transporter co-expressed in Xenopus oocytes. J Neurosci 17:4580-90.	
		Tanii Y, Nishikawa T, Hashimoto A, Takahashi K (1991): Stereoselective inhibition by D- and L-alanine of phencyclidine-induced locomotor stimulation in the rat. Brain Res 563:281-284.	
		Tanii Y, Hishikawa T, Hashimoto A, Takahashi K (1994): Stereoselective antagonism by enantiomers of alanine an dserien of phencyclidine-induced hyperactivity, stereotypy and ataxia. J. Pharmacol. Exp. Ther. 269:1040-1048.	
Ks		Tsai G, Yang P, Chung L -C, Lange N, Coyle J T (1998): D-serine in the treatment of schizophrenia. Biol. Psychiatry 44:1081-1089.	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov), MPEP 901.04 or in the comment box of this document. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to indicate here if English language Translation is attached.

Substitute for Form 1449 A & B/PTO		<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (Use as many sheets as necessary)		Application Number	10/066,657
		Confirmation Number	5724
		Filing Date	February 06, 2002
		First Named Inventor	Daniel JAVITT
		Art Unit	1617
		Examiner Name	Theodore J. Criares
Sheet <u>1</u> of <u>4</u>		Attorney Docket Number	A8311



U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. <sup>1</sup>	Document Number		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
		Number	Kind Code <sup>2</sup> (if known)		
		US			
		US			

FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document			Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Translation <sup>6</sup>
		Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>5</sup> (if known)			

NON PATENT LITERATURE DOCUMENTS
---------------------------------

K <sub>3</sub>		Wood P L (1995): The co-agonist concept: is the NMDA-associated glycine receptor saturated in vivo? Life Sci 57:301-10.	
K <sub>3</sub>		Wong E H, Knight A R, Ransom R (1987) Glycine modulates [3H]MK-801 binding to the NMDA receptor in rat brain. Eur J Pharmacol 142:487-8.	
K <sub>3</sub>		Zafra F, Aragon C, Olivares L, Danbolt N C, Gimenez C, Storm-Mathisen J (1995): Glycine transporters are differentially expressed among CNS cells. J Neurosci 15:3952-69.	
K <sub>3</sub>		Michael J. Schell, et al., "D-Serine as a neuromodulator: Regional and Developmental Localizations in Rat Brain Glia Resemble NMDA Receptors" The Journal of Neuroscience, March 1, 1997, 17(5):pg. 1604:1615.	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup>Applicant's unique citation designation number (optional). <sup>2</sup>See Kind Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov), MPEP 901.04 or in the comment box of this document. <sup>3</sup>Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). <sup>4</sup>For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup>Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup>Applicant is to indicate here if English language Translation is attached.